

REMARKS

Entry of the amendments and reconsideration of the rejection of the claims is respectfully requested.

Claims 31, 33-34, and 65 have been cancelled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

Claims 29-30, 32, 39-40, 48-49, 57-58, and 63-64 have been amended. Applicants submit the amended claims are supported throughout the specification including at page 7, line 26 to page 8, line 9, and Tables 2 and 3.

Claims 67 is new and is supported throughout the specification including at page 8, lines 1-7.

Claims 35 to 64 and 66 are withdrawn from consideration. Applicants submit that at least some of the claims are methods of using the polypeptides in the composition as claimed, and request rejoinder of the claims upon notice of allowable subject matter. Withdrawn claims 39-40, 48-49, 57-58, and 63-64 have been amended in order to be consistent with the substitute sequence listing submitted herewith.

Applicants have amended the specification to delete the sequence listing and enter the substitute sequence listing submitted herewith. Support for sequences 20 to 24 can be found throughout the specification including at Tables 2 and 3. Applicants have previously submitted an alignment showing the alignment of peptides having a sequence of SEQ ID NOs:2-11 with human sequences. The information in the alignment corresponds with that of Tables 2 and 3. Applicants note that they are also only filing the Substitute Sequence listing in electronic format. We understand that a paper copy of the Sequence Listing is no longer required.

35 USC 112, 2nd paragraph

The examiner rejected claims 29, 33, 34, and 65 under 35 USC 2nd paragraph for being indefinite. While not acquiescing to the rejection and solely to expedite prosecution, claims 33, 34, and 65 have been cancelled rendering the rejection of these claims moot. Applicants request withdrawal of this rejection.

35 USC 112, 1st paragraph

The examiner rejected claims 33, 34, and 65 under 35 USC 1st paragraph. While not acquiescing to the rejection and solely to expedite prosecution, claims 33, 34, and 65 have been cancelled rendering the rejection of these claims moot. Applicants request withdrawal of this rejection.

Applicants will discuss this rejection in so far as it might apply to claim 29 as amended. The examiner contends that the claims as amended on October 3, 2008 included SEQ ID NO:20,21,22,23,24,25,26,27,28,29, 30, 31, and 32 that are not described in the specification. Applicants respectfully traverse this rejection. Applicants submit that claim 29 as amended is supported in the specification in the least by the sequences in Tables 2 and 3. Applicants submit that claim 29 avoids a similar rejection.

35 USC 102

The Examiner rejected claims 29-32 under 35 USC 102 b in view of Vaughan-Thomas et al. Claim 31 has been cancelled rendering the rejection of this claim moot. Applicants traverse this rejection.

Applicants claim 29 is directed to a composition for treating or preventing arthritis or other degenerative disease, said composition comprising one or more polypeptides having at least 65% amino acid identity to SEQ ID NO: 14 and having an amino acid length of less than 250 amino acids, in combination with a physiological acceptable carrier, wherein said polypeptide induces tolerance to cartilage. Applicants submit that Vaughan-Thomas does not disclose a composition comprising a physiological carrier or one or more polypeptides having at least 65% amino acid identity to SEQ ID NO:14, wherein said polypeptide induces tolerance to cartilage. There is no discussion in this reference of compositions or of peptides that induce tolerance. For at least these reasons, Applicants submit that the Vaughan Thomas reference does not disclose all of the elements of the claims and therefore does not anticipate the claims. Applicants request withdrawal of this rejection.

35 USC 103

The examiner rejected claims 29-32 as unpatentable in view of Olsen et al. Applicants traverse this rejection.

The recent Supreme Court case, *KSR Int 'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727,

1734 (2007), sets forth the legal standard for obviousness. This case reaffirms the analytical framework set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), which mandates that an objective obviousness analysis includes: (1) determining the scope and content of the prior art; (2) ascertaining the differences between the prior art and the claims at issue; and (3) resolving the level of ordinary skill in the pertinent art. *Id.* at 1734. Secondary considerations such as commercial success, long felt but unsolved needs, or failure of others may also be persuasive.

In rejecting claims under 35 U.S.C. § 103(a), the examiner bears the initial burden of establishing a *prima facie* case of obviousness. *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992). Only if this initial burden is met does the burden of coming forward with evidence or argument shift to the appellant. *Id.* at 1445. Obviousness is then determined on the basis of the evidence as a whole and the relative persuasiveness of the arguments. *See Oetiker*, 977 F.2d at 1445. One criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that claimed subject matter should be carried out and would have a reasonable likelihood of success viewed in light of the prior art. *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988).

"It remains important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does". *KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1741 (2007). "Hindsight" is inferred when the specific understanding or principal within the knowledge of one of ordinary skill in the art leading to the modification of the prior art in order to arrive at appellant's claimed invention has not been explained. *In re Rouffet*, 149 F.3d 1350, 1358 (Fed. Cir. 1998). The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification. *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992). The claimed subject matter is nonobvious if it involves a number of complex and unpredictable alternatives and there is no reason one of skill in the art would select one alternative over another. *Ortho-McNeil vs. Mylan, Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008).

The combination of references must also suggest the claimed subject matter would have a reasonable likelihood of success. In the case of *Abbott Labs. v. Sandoz, Inc.*, the Federal Circuit stated:

"The court in *KSR* did not create a presumption that all experimentation in fields where there is already a background of useful knowledge is "obvious to try", without considering the nature of the science and technology. The methodology of science and the advance of technology are founded on the investigator's educated application of what is known, to intelligent exploration of what is not known. Each case must be decided in its particular context, including the characteristic of the science and technology, its state of advance, the nature of known choices, the specificity and generality of the prior art and the predictability of results in the area of interest." *Abbott Labs. v. Sandoz, Inc.*, 2008 U.S. App. LEXIS 21880 page 7 (Fed. Cir., Oct. 21, 2008).

The predictability of the art also impacts the assessment of whether solutions to the problem are predictable. As stated by the Fed. Cir in *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1355 (Fed. Cir. 2008):

"To the extent that an art is unpredictable, as the chemical arts often are, *KSR*'s focus on these "identified predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable."

Applicants submit that the *Olsen et al* reference does not disclose all of the elements of the claims or provide a reasonable expectation of success in obtaining the claimed subject matter. The *Olsen et al* reference does not disclose: a) a composition; b) comprising one or more polypeptides having at least 65% amino acid identity to SEQ ID NO: 14 and having an amino acid length of less than 250 amino acids, in combination with a physiological acceptable carrier, c) wherein said polypeptide induces tolerance to cartilage, and d) wherein the polypeptide comprises one or more polypeptide fragments selected from:

- (a) KSVFSYK (SEQ ID NO: 2);
- (b) QSVVFSYK (SEQ ID NO:20)
- (c) KIMIGVERS (SEQ ID NO: 3);
- (d) RIESLPIKPRG (SEQ ID NO: 5);
- (e) KHWSIWQIQDSSGKE (SEQ ID NO: 6);
- (f) KNWNIWQIQDSSGKE (SEQ ID NO:21)
- (g) RIGQDDLPGFDLISQFQIDKA (SEQ ID NO: 7);
- (h) RIGQDDLPGFDLISQFQVDKA (SEQ ID NO:22)
- (i) RHLYPNGLPEEYSFLTTFRM (SEQ ID NO: 8);
- (j) RNLYPSGLPEEYSFLTTFRM (SEQ ID NO:23);

- (k) KGLDGS LQTAAFSNLPSLFDSQWHKI (SEQ ID NO: 9);
(l) KGLDGS LQTAAFSNLSSLFDSQWHKI (SEQ ID NO:24); and
(m) RSSATL FVDCNRI [SEQ ID NO: 11].

Olsen does not describe a polypeptide having at least 65 % identity to SEQ ID NO:14 and that has less than 250 amino acids. Moreover, the polypeptides of Olsen et al are not described as inducing tolerance rather the only suggestion is such polypeptide might induce antibodies. In addition, the only polypeptide that has some sequence relationship to the peptides as disclosed by applicants does not disclose the entire fragment sequence. Thus, this reference does not disclose all of the elements of the claims.

In addition, there would be no reasonable expectation of success in obtaining applicants claimed subject matter as the peptide disclosed by Olsen was not shown to induce an antibody response; it was merely identified as a peptide that could be synthesized. In addition, there is not teaching or suggestion in this reference of the sequence identified by applicants. Finally, there is no teaching or suggestion that these peptides can or should be used to induce tolerance. The antibodies formed are only described as useful for diagnosis. Applicants, therefore submit that the one of skill in the art reading the Olsen reference would not have any reasonable expectation of success in obtaining the claimed subject matter.

Based on the foregoing, applicants request withdrawal of the 35 USC 103 rejection.

CONCLUSION

In view of the above amendments and remarks, Applicant respectfully requests notice of allowance of the claimed subject matter and rejoinder of method claims. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,
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